10553685

File 5:Biosis Previews(R) 1926-2008/Nov W3
(c) 2008 The Thomson Corporation

Set	Items	Description
? s Lingo and nogo		
	56	LINGO
	4384	NOGO
S1	29	LINGO AND NOGO

? t s1/7/1-29

1/7/1
DIALOG(R)File 5:Biosis Previews(R)

0020599486 BIOSIS NO.: 200800646425
Assessment of functional recovery and axonal sprouting in oligodendrocyte-myelin glycoprotein (OMgp) null mice after spinal cord injury
AUTHOR: Ji Benxiu; Case Lauren C; Liu Kai; Shao Zhaohui; Lee Xinhua; Yang Zhongshu; Wang Joy; Tian Tim; Shulga-Morskaya Svetlana; Scott Martin; He Zhigang; Relton Jane K; Mi Sha (Reprint)
AUTHOR ADDRESS: Biogen Idec Inc, Dept Discovery Biol, 14 Cambridge Ctr, Cambridge, MA 02142 USA**USA
AUTHOR E-MAIL ADDRESS: sha.mi@biogenidec.com
JOURNAL: Molecular and Cellular Neuroscience 39 (2): p258-267 OCT 2008 2008
ITEM IDENTIFIER: doi:10.1016/j.mcn.2008.07.004
ISSN: 1044-7431
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Oligodendrocyte-myelin glycoprotein (OMgp) is a myelin component that has been shown in vitro to inhibit neurite Outgrowth by binding to the %%%Nogo%%%-66 receptor (NgR1)/%%%Lingo%%%-1/Taj (TROY)/p75 receptor complex to activate the RhoA pathway. To investigate the effects of OMgp oil axon regeneration in vivo, OMgp(-/-) mice oil a mixed 129/Sv/C57BL/6 (129BL6) or a C57BL/6 (BL6) genetic background were tested in two spinal cord injury (SCI) models - a severe complete transection or a milder dorsal hemisection. OMgp(-/-) mice oil the mixed 129BL6 genetic background showed greater functional improvement compared to OMgp(-/-) littermates, with increased numbers of cholera toxin B-labeled ascending sensory axons and 5-HT+ descending axons and less RhoA activation after spinal cord injury. Myelin isolated from OMgp(-/-) mice (129BL6) was significantly less inhibitory to neurite outgrowth than wild-type (wt) myelin in vitro. However, OMgp(-/-) mice on a BL/6 genetic background showed neither statistically significant functional recovery nor axonal Sprouting following dorsal hemisection. (c) 2008 Elsevier Inc. All rights reserved.

1/7/2
DIALOG(R)File 5:Biosis Previews(R)

0020580872 BIOSIS NO.: 200800627811
%%%Nogo%%%-A and myelin-associated glycoprotein differently regulate oligodendrocyte maturation and myelin formation
AUTHOR: Pernet Vincent (Reprint); Joly Sandrine; Christ Franziska; Dimou Leda; Schwab Martin E
AUTHOR ADDRESS: Univ Zurich, Swiss Fed Inst Technol, Brain Res Inst, Winterthurerstr 190,Room 55J34A, CH-8057 Zurich, Switzerland**Switzerland
AUTHOR E-MAIL ADDRESS: pernet@hifo.uzh.ch
JOURNAL: Journal of Neuroscience 28 (29): p7435-7444 JUL 16 2008 2008
ITEM IDENTIFIER: doi:10.1523/JNEUROSCI.0727-08.2008
ISSN: 0270-6474
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: %%%Nogo%%%-A is one of the most potent oligodendrocyte-derived inhibitors for axonal regrowth in the injured adult CNS. However, the physiological function of %%%Nogo%%%-A in development and in healthy oligodendrocytes is still unknown. In the present study, we investigated the role of %%%Nogo%%%-A for myelin formation in the developing optic nerve. By quantitative real-time PCR, we found that the expression of %%%Nogo%%%-A increased faster in differentiating oligodendrocytes than that of the major myelin proteins MBP (myelin basic protein), PLP (proteolipid protein)/DM20, and CNP (2',3'-cyclic nucleotide 3'-phosphodiesterase). The analysis of optic nerves and cerebella of mice deficient for %%%Nogo%%%-A (%%%Nogo%%%-A(-/-)) revealed a marked delay of oligodendrocyte differentiation, myelin sheath formation, and axonal caliber growth within the first postnatal month. The combined deletion of %%%Nogo%%%-A and MAG caused a more severe transient hypomyelination. In contrast to MAG(-/-) mice, %%%Nogo%%%-A(-/-) mutants did not present abnormalities in the structure of myelin sheaths and Ranvier nodes. The common binding protein for %%%Nogo%%%-A and MAG, NgR1, was exclusively upregulated in MAG(-/-) animals, whereas the level of %%%Lingo%%%-1, a coreceptor, remained unchanged. Together, our results demonstrate that %%%Nogo%%%-A and MAG are differently involved in oligodendrocyte maturation in vivo, and suggest that %%%Nogo%%%-A may influence also remyelination in pathological conditions such as multiple sclerosis.

1/7/3

0020485118 BIOSIS NO.: 200800532057
Inactivation of glycogen synthase kinase-3 beta and up-regulation of %%%LINGO%%%-1 are involved in %%%LINGO%%%-1 antagonist regulated survival of cerebellar granular neurons
AUTHOR: Zhao Xiang-Hui; Jin Wei-Lin (Reprint); Wu Jiang; Mi Sha; Ju Gong
AUTHOR ADDRESS: Shanghai Jiao Tong Univ, Inst Neurosci, 800 Dongchuan Rd, Shanghai 200240, Peoples R China**Peoples R China
AUTHOR E-MAIL ADDRESS: weilinjin@yahoo.com; jugong@fmmu.edu.cn
JOURNAL: Cellular and Molecular Neurobiology 28 (5): p727-735 AUG 2008 2008
ITEM IDENTIFIER: doi:10.1007/s10571-007-9258-6
ISSN: 0272-4340
DOCUMENT TYPE: Article

RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: %%%LINGO%%%-1 has been critically implicated in the central regulation of CNS axon regeneration and oligodendrocyte maturation. We have recently demonstrated that pretreatment with %%%LINGO%%%-1 antagonist (%%%LINGO%%%-1-Fc) inhibited low potassium-induced cerebellar granular neurons (CGNs) apoptosis. In the present study, we examined the neuroprotective mechanism of %%%LINGO%%%-1-Fc by Western blot and in situ GST pull-down assay. CGN cultures were preincubated in medium with %%%LINGO%%%-1-Fc or control protein at the concentration of 10 mu g/ml for 2 h and then switched to low potassium medium in the presence of corresponding proteins. Cultures were harvested at indicated time intervals for successive analysis. Several apoptosis-associated signaling factors, GSK-3 beta, ERK1/2, and Rho GTPases, were observed to be activated in response to potassium deprivation and the activation/dephosphorylation of GSK-3 beta was suppressed by %%%LINGO%%% -1-Fc pretreatment compared with control group. Besides, the endogenous %%%LINGO%%%-1 expression level of CGN cultures was augmented by low potassium stimuli and restrained by %%%LINGO%%%-1 antagonist treatment. Although the protein level of p75(NTR) and %%%Nogo%%%-A were down-regulated in different patterns during apoptosis, neither of them was affected by %%%LINGO%%%-1-Fc application. Taken together, these results suggest a new mechanism of %%%LINGO%%%-1 antagonist regulated neuronal survival involving protein synthesis of %%%LINGO%%%-1 and inactivation of GSK-3 pathway.

1/7/4
DIALOG(R)File 5:Biosis Previews(R)

0020445995 BIOSIS NO.: 200800492934
Depending on dose and context, alcohol consumption can both increase and decrease hippocampal neurogenesis in rodents
AUTHOR: Aberg E (Reprint); Olson L; Brene S
AUTHOR ADDRESS: Karolinska Inst, Dept Neurosci, Stockholm, Sweden**Sweden
JOURNAL: Alcoholism Clinical and Experimental Research 32 (6, Suppl. 1): p 277A JUN 2008 2008
CONFERENCE/MEETING: Joint Scientific Meeting of the Research-Society-on-Alcoholism and the International-Society-for-Biomedical-Research-on-Alcoholism Washington, DC, USA June 27 -July 02, 2008; 20080627
SPONSOR: Res Soc Alcoholism
Int Soc Biomed Res Alcoholism
ISSN: 0145-6008
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

1/7/5
DIALOG(R)File 5:Biosis Previews(R)

0020413664 BIOSIS NO.: 200800460603
Functional MRI and MRS to monitor sensory function and plasticity in

experimental spinal cord injury
AUTHOR: Olson L (Reprint)
AUTHOR ADDRESS: Karolinska Inst, Dept Neurosci, Stockholm, Sweden**Sweden
JOURNAL: Cell Transplantation 17 (4): p477-478 2008 2008
CONFERENCE/MEETING: 15th Annual Meeting of the
American-Society-for-Neural-Therapy-and-Repair Clearwater Beach, FL, USA
May 01 -03, 2008; 20080501
SPONSOR: Amer Soc Neural Therapy & Repair
ISSN: 0963-6897
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

1/7/6
DIALOG(R)File 5:Biosis Previews(R)

0020208860 BIOSIS NO.: 200800255799
Developmental analysis of %%%Lingo%%%-1/Lern1 protein expression in the mouse brain: Interaction of its intracellular domain with Myt1l
AUTHOR: Llorens Franc; Gil Vanesa; Iraola Susana; Carim-Todd Laura; Marti Eulalia; Estivill Xavier; Soriano Eduardo; del Rio Jose Antonio; Sumoy Lauro (Reprint)
AUTHOR ADDRESS: UPF, CRG, Bioinformat and Genom Program, Barcelona 08003, Spain**Spain
AUTHOR E-MAIL ADDRESS: lauro.sumoy@crg.es
JOURNAL: Developmental Neurobiology 68 (4): p521-541 MAR 2008 2008
ITEM IDENTIFIER: doi:10.1002/dneu.20607
ISSN: 1932-8451_(print) 1932-846X_(electronic)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: %%%Lingo%%%-1 (also known as Lern1) is a component of the %%%Nogo%%% receptor complex that mediates intracellular signaling in response to myelin associated inhibitors (MAIs): NogoA, MAG, and Omgp. Signaling through %%%Nogo%%% receptor extends to more than its well known role in preventing axon regeneration after lesion in the CNS, being implicated in neuronal functional maturation. Using %%%Lingo%%% -1-deficient mice, it has been demonstrated that %%%Lingo%%%-1 plays relevant roles in oligodendrocyte differentiation during brain development, and that treatment with %%%Lingo%%%-1 antagonists can improve axon regeneration after lesion in adult mice by decreasing MAI mediated signaling. However, a detailed description of the pattern of expression of %%%Lingo%%%-1 protein in correlation with the other partners of %%%Nogo%%% receptor is missing. Here, we show that components of the %%%Nogo%%% receptor complex, %%%Lingo%%%-1, NgR1, p75, and TROY coexist in mouse brain in a defined time window only at later postnatal stages. We have also determined the %%%Lingo%%%-1 distribution showing expression in particular subsets of neurons, but not in myelinating mature oligodendrocytes. Surprisingly, %%%Lingo%%%-1 is expressed at early developmental stages without NgR1, which supports the notion that %%%Lingo%%%-1 may participate in other activities in developing neurons different from oligodendrocyte maturation or axon extension inhibition in the adult. Finally, we propose that the intracellular domain of %%%Lingo%%%-1 contributes to signaling and show that it interacts with

the postmitotic neuronal specitic zinc finger protein Myt1l, suggesting that %%%Lingo%%%-1 may regulate Myt1l transcription factor activity by affecting its subcellular localization. (C) 2008 Wiley Periodicals, Inc.

1/7/7
DIALOG(R)File 5:Biosis Previews(R)

0020098117 BIOSIS NO.: 200800145056
Molecular mechanism and regulation of axon growth inhibition
AUTHOR: Yamashita Toshihide (Reprint)
AUTHOR ADDRESS: Chiba Univ, Dept Neurobiol, Grad Sch Med, Chuo Ku, 1-8-1 Inohana, Chiba 2608670, Japan**Japan
JOURNAL: Brain and Nerve (Tokyo) 59 (12): p1347-1353 DEC 2007 2007
ISSN: 1881-6096
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: Japanese

ABSTRACT: In the adult mammalian central nervous system (CNS), it is well known that injured axons exhibit very limited regeneration ability. Due to this lack of appropriate axonal regeneration, a traumatic damage to the adult brain and spinal cord frequently causes permanent neuronal deficits such as paralysis. Several axon growth inhibitors, including myelin-associated glycoprotein, %%%Nogo%%%, and oligodensrocyte myelin glycoprotein, in the CNS have been identified in the myelin. Receptor complex comprising of the %%%Nogo%%% receptor, the p75 receptor, and %%%LINGO%%%-1 transduces the signals from all of these inhibitors in. vitro. Downstream of these inhibitors, activation of small GTPase RhoA and its effector Rho-kinase has been shown to be a key element for neurite growth inhibition and growth cone collapse elicited by these inhibitors. Consistent with these findings in, vitro, inhibition of RhoA or Rho-kinase in. vivo promotes axon growth and functional recovery after spinal cord injury. Recently, several developmental guidance proteins, including repulsive guidance molecules, semaphorin, and ephrin are suggested to be involved in axon growth inhibition after injury to the CNS. Thus, multiple axon growth inhibitors seem to contribute to inability of the injured axons to regenerate, and therapeutic strategy to block the multiple axon growth inhibitors may provide efficient tools that produce functional regeneration following injuries to the CNS. In addition, it is noted that synaptic plasticity in pre-existing pathways and the formation of new circuits through collateral sprouting of lesioned and unlesioned fibers are important components of the spontaneous recovery process. The molecular mechanism of this phenomenon is poorly understood, and elucidation of this will contribute to enhancement of functional recovery after incomplete injury to the CNS. I will summarize recent findings regarding these issues.

1/7/8
DIALOG(R)File 5:Biosis Previews(R)

0020018862 BIOSIS NO.: 200800065801
%%%LINGO%%%-1 antagonist promotes spinal cord remyelination and axonal integrity in MOG-induced experimental autoimmune encephalomyelitis

AUTHOR: Mi Sha (Reprint); Hu Bing; Hahm Kyungmin; Luo Yi; Hui Edward Sai Kam; Yuan Qiuju; Wong Wai Man; Wang Li; Su Huanxing; Chu Tak-Ho; Guo Jiasong; Zhang Wenming; So Kwok-Fai; Pepinsky Blake; Shao Zhaohui; Graff Christilyn; Garber Ellen; Jung Vincent; Wu Ed Xuekui; Wu Wutian
AUTHOR ADDRESS: Biogen Idec Inc, 14 Cambridge Ctr, Cambridge, MA 02142 USA **USA
AUTHOR E-MAIL ADDRESS: sha.mi@biogenidec.com; wtwu@hkucc.hku.hk
JOURNAL: Nature Medicine 13 (10): p1228-1233 OCT 2007 2007
ITEM IDENTIFIER: doi:10.1038/nm1664
ISSN: 1078-8956
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Demyelinating diseases, such as multiple sclerosis, are characterized by the loss of the myelin sheath around neurons, owing to inflammation and gliosis in the central nervous system (CNS). Current treatments therefore target anti- inflammatory mechanisms to impede or slow disease progression. The identification of a means to enhance axon myelination would present new therapeutic approaches to inhibit and possibly reverse disease progression. Previously, LRR and Ig domain - containing, %%%Nogo%%% receptor interacting protein (%%%LINGO%%%- 1) has been identified as an in vitro and in vivo negative regulator of oligodendrocyte differentiation and myelination. Here we show that loss of %%%LINGO%%%- 1 function by Lingo1 gene knockout or by treatment with an antibody antagonist of %%%LINGO%%%- 1 function leads to functional recovery from experimental autoimmune encephalomyelitis. This is reflected biologically by improved axonal integrity, as confirmed by magnetic resonance diffusion tensor imaging, and by newly formed myelin sheaths, as determined by electron microscopy. Antagonism of %%%LINGO%%%- 1 or its pathway is therefore a promising approach for the treatment of demyelinating diseases of the CNS.

1/7/9
DIALOG(R)File 5:Biosis Previews(R)

0019998334 BIOSIS NO.: 200800045273
Targeting the %%%Nogo%%%-A signalling pathway to promote recovery following acute CNS injury
AUTHOR: Walmsey A R (Reprint); Mir A K
AUTHOR ADDRESS: Novartis Inst Biomed Res, CH-4056 Basel, Switzerland** Switzerland
AUTHOR E-MAIL ADDRESS: adrianrobert.walmsley@novartis.com
JOURNAL: Current Pharmaceutical Design 13 (24): p2470-2484 2007 2007
ISSN: 1381-6128
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Functional recovery following acute CNS injury in humans, such as spinal cord injury and stroke, is exceptionally limited, leaving the affected individual with life-long neurological deficits such as loss of limb movement and sensation leading to a compromised quality of life. As yet, there is no effective treatment on the market for such injuries. This lack of functional recovery can at least in part be attributed to

the restriction of axonal regeneration and neuroplasticity by several CNS myelin proteins that have been shown to be potent inhibitors of neurite outgrowth in vitro, namely myelin-associated glycoprotein (MAG), %%%Nogo%%%-A and oligodendrocyte myelin glycoprotein (OMgp). %%%Nogo%%%-A contains multiple neurite outgrowth inhibitory domains exposed on the surface of myelinating oligodendrocytes located within its amino-terminal region (amino-%%%Nogo%%%-A) and C-terminal region (%%%Nogo%%%-66). Although structurally dissimilar; %%%Nogo%%%-66, MAG and OMgp exert their inhibitory effects by binding the GPI-linked neuronal %%%Nogo%%%-66 receptor (NgR) that transduces the inhibitory signal to the cell interior via transmembrane co-receptors %%%LINGO%%%-1 and p75(NTR) R or TROY. Although the receptor(s) for amino-%%%Nogo%%%-A are unknown, amino-%%%Nogo%%%-A and NgR ligands mutually activate the small GTPase RhoA. Consistent with their neurite outgrowth inhibitory function, approaches counter-acting %%%Nogo%%%-A using function-blocking antibodies, NgR using peptide antagonists and receptor bodies or RhoA using deactivating enzymes have been shown to significantly enhance axonal regeneration and neuroplasticity leading to improved functional recovery in animal models of acute CNS injury. These in vivo findings thus provide a sound basis for the development of an effective treatment for acute CNS injuries in humans.

1/7/10
DIALOG(R)File 5:Biosis Previews(R)

0019997650 BIOSIS NO.: 200800044589
Cortical sensory map rearrangement after spinal cord injury: fMRI responses linked to %%%Nogo%%% signalling
AUTHOR: Endo Toshiki (Reprint); Spenger Christian; Tominaga Teiji; Brene Stefan; Olson Lars
AUTHOR ADDRESS: Karolinska Inst, Dept Neurosci, Retzius Vag 8, S-17177 Stockholm, Sweden**Sweden
AUTHOR E-MAIL ADDRESS: toshiki.endo@ki.se
JOURNAL: Brain 130 (Part 11): p2951-2961 NOV 2007 2007
ITEM IDENTIFIER: doi:10.1093/brain/awm237
ISSN: 0006-8950
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Cortical sensory maps can reorganize in the adult brain in an experience-dependent manner. We monitored somatosensory cortical reorganization after sensory deafferentation using functional magnetic resonance imaging (fMRI) in rats subjected to complete transection of the mid-thoracic spinal cord. Cortical representation in response to spared forelimb stimulation was observed to enlarge and invade adjacent sensory-deprived hind limb territory in the primary somatosensory cortex as early as 3 days after injury. Functional MRI also demonstrated long-term cortical plasticity accompanied by increased thalamic activation. To support the notion that alterations of cortical neuronal circuitry after spinal cord injury may underlie the fMRI changes, we quantified transcriptional activities of several genes related to cortical plasticity including the %%%Nogo%%% receptor (NgR), its co-receptor %%%LINGO%%%-1 and brain derived neurotrophic factor (BDNF), using in situ hybridization. We demonstrate that NgR and %%%LINGO%%%-1

are down-regulated specifically in cortical areas deprived of sensory input and in adjacent cortex from 1 day after injury, while BDNF is up-regulated. Our results demonstrate that cortical neurons react to sensory deprivation by decreasing transcriptional activities of genes encoding the %%%Nogo%%% receptor components in the sensory deprived and the anatomically adjacent non-deprived area. Combined with the BDNF up-regulation, these changes presumably allow structural changes in the neuropil. Our observations therefore suggest an involvement of %%%Nogo%%% signalling in cortical activity-dependent plasticity in the somatosensory system. In spinal cord injury, cortical reorganization as shown here can become a disadvantage, much like the situation in amblyopia or phantom sensation. Successful strategies to repair sensory pathways at the spinal cord level may not lead to proper reestablishment of cortical connections, once deprived hind limb cortical areas have been reallocated to forelimb use. In such situations, methods to control cortical plasticity, possibly by targeting %%%Nogo%%% signalling, may become helpful.

0019923458 BIOSIS NO.: 200700583199
Inhibition of the leucine-rich repeat protein %%%LINGO%%%-1 enhances survival, structure, and function of dopaminergic neurons in Parkinson's disease models
AUTHOR: Inoue Haruhisa; Lin Ling; Lee Xinhua; Shao Zhaohui; Mendes Shannon; Snodgrass-Belt Pamela; Sweigard Harry; Engber Tom; Pepinsky Blake; Yang Lichuan; Beal M Flint; Mi Sha; Isacson Ole (Reprint)
AUTHOR ADDRESS: Biogen Idec Inc, Dept Discovery Biol, 14 Cambridge Ctr, Cambridge, MA 02142 USA**USA
AUTHOR E-MAIL ADDRESS: isacson@hms.harvard.edu
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 104 (36): p14430-14435 SEP 4 2007 2007
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The nervous system-specific leucine-rich repeat Ig-containing protein %%%LINGO%%%-1 is associated with the %%%Nogo%%%-66 receptor complex and is endowed with a canonical EGF receptor (EGFR)-like tyrosine phosphorylation site. Our studies indicate that %%%LINGO%%%-1 expression is elevated in the substantial nigra of Parkinson's disease (PD) patients compared with age-matched controls and in animal models of PD after neurotoxic lesions. %%%LINGO%%%-1 expression is present in midbrain dopaminergic (DA) neurons in the human and rodent brain. Therefore, the role of %%%LINGO%%%-1 in cell damage responses of DA neurons was examined in vitro and in experimental models of PD induced by either oxidative (6-hydroxydopamine) or mitochondrial (N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) toxicity. In %%%LINGO%%%-1 knockout mice, DA neuron survival was increased and behavioral abnormalities were reduced compared with WT. This neuroprotection was accompanied by increased Akt phosphorylation (p-Akt). Similar neuroprotective in vivo effects on midbrain DA neurons were obtained in WT mice by blocking %%%LINGO%%%-1 activity using %%%LINGO%%%-1-Fc

protein. Neuroprotection and enhanced neurite growth were also demonstrated for midbrain DA neurons in vitro. %%%LINGO%%%-1 antagonists (%%%LINGO%%%-1-Fc, dominant negative %%%LINGO%%%-1, and anti-%%%LINGO%%%-1 antibody) improved DA neuron survival in response to MPP+ in part by mechanisms that involve activation of the EGFR/Akt signaling pathway through a direct inhibition of LINGO1's binding to EGFR. These results show that inhibitory agents of %%%LINGO%%%-1 activity can protect DA neurons against degeneration and indicate a role for the leucine-rich repeat protein %%%LINGO%%%-1 and related classes of proteins in the pathophysiological responses of midbrain DA neurons in PD.

1/7/12
DIALOG(R)File 5:Biosis Previews(R)

0019921810 BIOSIS NO.: 200700581551
An in vitro study on the involvement of %%%LINGO%%%-1 and Rho GTPases in %%%Nogo%%%-A regulated differentiation of oligodendrocyte precursor cells
AUTHOR: Zhao Xiang-Hui; Jin Wei-Lin; Ju Gong (Reprint)
AUTHOR ADDRESS: Fourth Mil Med Univ, Inst Neurosci, 17 Chang Le Xi Rd, Xian 710032, Peoples R China**Peoples R China
AUTHOR E-MAIL ADDRESS: weilinjin@yahoo.com; jugong@fmmu.edu.cn
JOURNAL: Molecular and Cellular Neuroscience 36 (2): p260-269 OCT 2007 2007
ITEM IDENTIFIER: doi:10.1016/j.mcn.2007.07.008
ISSN: 1044-7431
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: %%%Nogo%%%-A has been considered as one of the most important myelin-associated axonal regeneration inhibitors in the central nervous system. Recent studies have demonstrated various additional physiological roles of %%%Nogo%%% family members. To understand the possible effect of %%%Nogo%%%-A on the differentiation of oligodendrocytes, antibodies against distinct extracellular domains of %%%Nogo%%%-A were applied in cell cultures. Oligodendrocyte precursor cells from P2 rat cortex were grown in the presence of monoclonal antibody against the N-terminal inhibitory domain of %%%Nogo%%%-A or the C-terminal 66 amino acid loop of %%%Nogo%%%-A for 3 days, and the antibody treatment resulted in stunted process extension and inhibited differentiation of oligodendrocytes. Concomitant with morphology changes, Rho GTPases activity was greatly increased upon the antibody treatment and the expression level of %%%LINGO%%%-1, which was recently shown to be a negative regulator for the oligodendrocyte maturation, was upregulated in the process of antibody treatment. These results indicate that endogenous %%%Nogo%%%-A expressed in oligodendrocyte may act though Rho GTPase and %%%LINGO%%%-I to influence the morphological differentiation of oligodendrocytes and will help us to understand the physiology role of %%%Nogo%%%-A in oligodendrocyte biology. (c) 2007 Elsevier Inc. All rights reserved.

1/7/13
DIALOG(R)File 5:Biosis Previews(R)

0019777519 BIOSIS NO.: 200700437260
Roles of glial p75NTR in axonal regeneration
AUTHOR: Zhou Xin-Fu (Reprint); Li Hong-Yun
AUTHOR ADDRESS: Flinders Univ S Australia, Ctr Neurosci, Dept Human Physiol, Adelaide, SA 5001, Australia**Australia
AUTHOR E-MAIL ADDRESS: xin-fu.zhou@flinders.edu.au
JOURNAL: Journal of Neuroscience Research 85 (8): p1601-1605 JUN 2007 2007
ITEM IDENTIFIER: doi:10.1002/jnr.21220
ISSN: 0360-4012
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The neurotrophin receptor p75 (p75NTR) is expressed by both neurons and glia. Nerve injury triggers up-regulation of p75NTR in Schwann cells (SC) but not in central glia. In contrast to neuronal p75NTR, which mediates negative signals from myelin-associated proteins resulting in neurite collapse, glial p75NTR may play a positive role in nerve regeneration by forming neurotrophin chemoattractant gradients or by competitively antagonizing the %%%NOGO%%%/NgR/%%%LINGO%%%-1 signal through cell-cell contact or regulated intramembranous proteolysis (RIP) of p75NTR. This piece presents some recent evidence supporting this hypothesis. (c) 2007Wiley-Liss, Inc.

1/7/14
DIALOG(R)File 5:Biosis Previews(R)

0019455840 BIOSIS NO.: 200700115581
TROY and %%%LINGO%%%-1 expression in astrocytes and macrophages/microglia in multiple sclerosis lesions
AUTHOR: Satoh J (Reprint); Tabunoki H; Yamamura T; Arima K; Konno H
AUTHOR ADDRESS: Meiji Pharmaceut Univ, Dept Bioinformat, 2-522-1 Noshio, Tokyo 2048588, Japan**Japan
AUTHOR E-MAIL ADDRESS: satoj@my-pharm.ac.jp
JOURNAL: Neuropathology and Applied Neurobiology 33 (1): p99-107 FEB 2007 2007
ISSN: 0305-1846
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: %%%Nogo%%% constitutes a family of neurite outgrowth inhibitors contributing to a failure of axonal regeneration in the adult central nervous system (CNS). %%%Nogo%%%-A is expressed exclusively on oligodendrocytes where %%%Nogo%%%-66 segment binds to %%%Nogo%%% receptor (NgR) expressed on neuronal axons. NgR signalling requires a coreceptor p75(NTR) or TROY in combination with an adaptor %%%LINGO%%%-1. To characterize the cell types expressing the NgR complex in the human CNS, we studied demyelinating lesions of multiple sclerosis (MS) brains by immunohistochemistry. TROY and %%%LINGO%%%-1 were identified in subpopulations of reactive astrocytes, macrophages/microglia and neurones but not in oligodendrocytes. TROY was up-regulated, whereas %%%LINGO%%%-1 was reduced in MS brains by Western blot. These results suggest that the ternary complex of NgR/TROY/%%%LINGO%%%-1 expressed on astrocytes, macrophages/microglia and neurones, by interacting with %%%Nogo%%%-A on

oligodendrocytes, might modulate glial-neuronal interactions in demyelinating lesions of MS.

1/7/15
DIALOG(R)File 5:Biosis Previews(R)

0019444746 BIOSIS NO.: 200700104487
NGF regulates the expression of axonal %%%LINGO%%%-1 to inhibit oligodendrocyte differentiation and myelination
AUTHOR: Lee Xinhua; Yang Zhongshu; Shao Zhaohui; Rosenberg Sheila S; Levesque Melissa; Pepinsky R Blake; Qiu Mengsheng; Miller Robert H; Chan Jonah R (Reprint); Mi Sha
AUTHOR ADDRESS: Univ So Calif, Keck Sch Med, Zilkha Neurogenet Inst, Dept Cell and Neurobiol, Los Angeles, CA 90033 USA**USA
AUTHOR E-MAIL ADDRESS: jonah.chan@usc.edu; sha.mi@biogenidec.com
JOURNAL: Journal of Neuroscience 27 (1): p220-225 JAN 3 2007 2007
ISSN: 0270-6474
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Neurons and glia share a mutual dependence in establishing a functional relationship, and none is more evident than the process by which axons control myelination. Here, we identify LRR and Ig domain-containing, %%%Nogo%%% receptor-interacting protein (%%%LINGO%%%-1) as a potent axonal inhibitor of oligodendrocyte differentiation and myelination that is regulated by nerve growth factor and its cognate receptor TrkA in a dose-dependent manner. Whereas %%%LINGO%%%-1 expressed by oligodendrocyte progenitor cells was previously identified as an inhibitor of differentiation, we demonstrate that axonal expression of %%%LINGO%%%-1 inhibits differentiation with equal potency. Disruption of %%%LINGO%%%-1 on either cell type is sufficient to overcome the inhibitory action and promote differentiation and myelination, independent of axon diameter. Furthermore, these results were recapitulated in transgenic mice overexpressing the full length %%%LINGO%%%-1 under the neuronal promoter synapsin. Myelination was greatly inhibited in the presence of enforced axonal %%%LINGO%%%-1. The implications of these results relate specifically to the development of potential therapeutics targeting extrinsic growth factors that may regulate the axonal expression of modulators of oligodendrocyte development.

1/7/16
DIALOG(R)File 5:Biosis Previews(R)

19413444 BIOSIS NO.: 200700073185
The structure of the %%%Lingo%%%-1 ectodomain, a module implicated in central nervous system repair inhibition
AUTHOR: Mosyak Lidia (Reprint); Wood Andrew; Dwyer Brian; Buddha Madhavan; Johnson Mark; Aulabaugh Ann; Zhong Xiaotian; Presman Eleonora; Benard Susan; Kelleher Kerry; Wilhelm James; Stahl Mark L; Kriz Ron; Gao Ying; Cao Zixuan; Ling Huai-Ping; Pangalos Menelas N; Walsh Frank S; Somers William S

AUTHOR ADDRESS: Wyeth Res, Dept Chem and Screening Sci, 200 Cambridge Pk Dr, Cambridge, MA 02140 USA**USA
AUTHOR E-MAIL ADDRESS: lmosyak@wyeth.com; wsomers@wyeth.com
JOURNAL: Journal of Biological Chemistry 281 (47): p36378-36390 NOV 24 2006 2006
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: %%%Nogo%%% receptor (NgR)-mediated control of axon growth relies on the central nervous system-specific type I transmembrane protein %%%Lingo%%%-1. Interactions between %%%Lingo%%%-1 and NgR, along with a complementary co-receptor, result in neurite and axonal collapse. In addition, the inhibitory role of %%%Lingo%%%-1 is particularly important in regulation of oligodendrocyte differentiation and myelination, suggesting that pharmacological modulation of %%%Lingo%%%-1 function could be a novel approach for nerve repair and remyelination therapies. Here we report on the crystal structure of the ligand-binding ectodomain of human %%%Lingo%%%-1 and show it has a bimodular, kinked structure composed of leucine-rich repeat (LRR) and immunoglobulin (Ig)-like modules. The structure, together with biophysical analysis of its solution properties, reveals that in the crystals and in solution %%%Lingo%%%-1 persistently associates with itself to form a stable tetramer and that it is its LRR-Ig-composite fold that drives such assembly. Specifically, in the crystal structure protomers of %%%Lingo%%%-1 associate in a ring-shaped tetramer, with each LRR domain filling an open cleft in an adjacent protomer. The tetramer buries a large surface area (9,200 A 2) and may serve as an efficient scaffold to simultaneously bind and assemble the NgR complex components during activation on a membrane. Potential functional binding sites that can be identified on the ectodomain surface, including the site of self-recognition, suggest a model for protein assembly on the membrane.

1/7/17

19357031 BIOSIS NO.: 200700016772
%%%LINGO%%%-1 antagonist promotes functional recovery and axonal sprouting after spinal cord injury
AUTHOR: Ji Benxiu; Li Mingwei; Wu Wu-Tian; Yick Leung-Wah; Lee Xinhua; Shao Zhaohui; Wang Joy; So Kwok-Fai; McCoy John M; Pepinsky R Blake; Mi Sha (Reprint); Relton Jane K
AUTHOR ADDRESS: Biogen Inc, 14 Cambridge Ctr, Cambridge, MA 02142 USA**USA
AUTHOR E-MAIL ADDRESS: sha.mi@biogenidec.com
JOURNAL: Molecular and Cellular Neuroscience 33 (3): p311-320 NOV 2006 2006
ISSN: 1044-7431
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: %%%LINGO%%%-1 is a CNS-specific protein and a functional component of the NgR1/p75/%%%LINGO%%%-1 and NgR1/TAJ(TROY)/%%%LINGO%%%-1 signaling complexes that mediate inhibition of axonal outgrowth. These

receptor complexes mediate the axonal growth inhibitory effects of %%%Nogo%%%, myelin-associated glycoprotein (MAG) and oligodendrocyte-myelin glycoprotein (OMgp) via RhoA activation. Soluble %%%LINGO%%%-1 (%%%LINGO%%%-1-Fc), which acts as an antagonist of these pathways by blocking %%%LINGO%%%-1 binding to NgR1, was administered to rats after dorsal or lateral hemisection of the spinal cord. %%%LINGO%%%-1-Fc treatment significantly improved functional recovery, promoted axonal sprouting and decreased RhoA activation and increased oligodendrocyte and neuronal survival after either rubrospinal or corticospinal tract transection. These experiments demonstrate an important role for %%%LINGO%%%-1 in modulating axonal outgrowth in vivo and that treatment with %%%LINGO%%%-1-Fc can significantly enhance recovery after spinal cord injury.

1/7/18
DIALOG(R)File 5:Biosis Previews(R)

19352928 BIOSIS NO.: 200700012669
TACE-induced cleavage of NgR and p75(NTR) in dorsal root ganglion cultures disinhibits outgrowth and promotes branching of neurites in the presence of inhibitory CNS myelin
AUTHOR: Ahmed Zubair; Mazibrada Gordon; Seabright Ruth J; Dent Russell G; Berry Martin; Logan Ann (Reprint)
AUTHOR ADDRESS: Univ Birmingham, Div Med Sci, Mol Neurosci Grp, Birmingham B15 2TT, W Midlands, UK**UK
AUTHOR E-MAIL ADDRESS: a.logan@bham.ac.uk
JOURNAL: FASEB Journal 20 (11): SEP 2006 2006
ISSN: 0892-6638
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: After binding, central nervous system (CNS) myelin-derived axon growth inhibitory ligands, the %%%Nogo%%%-66 receptor (NgR), complexes with %%%LINGO%%%-1 and either the low-affinity neurotrophin receptor (p75(NTR)) or TROY to initiate growth cone collapse via a Rho-A inhibitory signaling pathway and/or Ca2+-dependent activation of epidermal growth factor receptor (EGFR) through an unknown signaling pathway. We have shown that axon growth through CNS myelin is disinhibited after neurotrophic factor administration by 1) initiating intramembranous proteolysis (RIP) of p75NTR, leading to cleavage of the extracellular (p75(ECD)) and intracellular domains (p75(ICD)) by alpha- and gamma-secretase, respectively, thereby paralyzing inhibitory signaling; 2) shedding of soluble NgR(ECD), which acts as a competitive antagonist to NgR for binding of inhibitory ligands; and 3) antagonizing NgR/p75(NTR) clustering by competitive p75(ECD)/NgR interaction. Here, we report that TNF-alpha converting enzyme (TACE) (a disintegrin and metalloproteinase 17, ADAM17) induces disinhibition of FGF2-stimulated neurite outgrowth of dorsal root ganglion neurons (DRGN) cultured in the presence of a predetermined concentration of inhibitory CNS myelin-derived ligands. After addition of TACE (which has alpha-secretase activity) to mitotically arrested adult rat mixed DRG cultures, we demonstrate 1) NgRECD shedding; 2) release of p75ECD and p75ICD by RIP of p75NTR; 3) blockade of Rho-A activation; 4) reduced EGFR phosphorylation;

and 5) increased FGF2-stimulated DRGN neurite outgrowth and branching in the presence of CNS myelin-derived inhibitory ligands. Thus, TACE-induced cleavage of NgR and RIP of p75NTR abrogates axon growth inhibitory signaling, thereby disinhibiting CNS axon/neurite growth.

1/7/19
DIALOG(R)File 5:Biosis Previews(R)

19044062 BIOSIS NO.: 200600389457
AMIGO and friends: An emerging family of brain-enriched, neuronal growth modulating, type I transmembrane proteins with leucine-rich repeats (LRR) and cell adhesion molecule motifs
AUTHOR: Chen Yanan; Aulia Selina; Li Lingzhi; Tang Bor Luen (Reprint)
AUTHOR ADDRESS: Natl Univ Singapore, Dept Biochem, 8 Med Dr, Singapore 117597, Singapore**Singapore
AUTHOR E-MAIL ADDRESS: bchtbl@nus.edu.sg
JOURNAL: Brain Research Reviews 51 (2): p265-274 AUG 2006 2006
ISSN: 0165-0173
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Leucine-rich repeats (LRR) are protein-protein interaction domains (20-29 amino acid residues in length) found in proteins with diverse structure and functions. We note here an emerging group of central nervous system-enriched, type I surface proteins with an ectodomain containing LRR repeats and motifs found in cell adhesion molecules. Members of this group include the Amphoterin-induced gene and ORF-1 (AMIGO-1), LRR and Ig domain containing %%%Nogo%%% Receptor interacting protein I (%%%LINGO%%%-1) and the netrin-G1 ligand NGL-1. The above proteins carry, in addition to the LRR repeats, an immunoglobin (Ig)-like segment in their ectodomain. Two other related families of molecules, the NLRRs and the FLRTs, have in addition, a fibronectin type III repeat. The LRR domain distinguishes these molecules from the more extensively studied Ig-like family of cell adhesion molecules, and the transmembrane domain differentiate them from the family of secreted extracellular proteoglycans with LRRs. Functionally, many members of this group of proteins could modulate neurite outgrowth of neurons, at least in vitro. %%%LINGO%%%-1, initially discovered as a component of the %%%Nogo%%%-66 receptor complex which inhibits neurite growth, also regulates oligodendrocyte differentiation and myelination. Current knowledge and recent findings pertaining to the functions of this interesting group of proteins in the nervous system are discussed. (c) 2005 Elsevier B.V. All rights reserved

1/7/20
DIALOG(R)File 5:Biosis Previews(R)

19039503 BIOSIS NO.: 200600384898
Selective decline of %%%Nogo%%% mRNA in the aging brain
AUTHOR: Trifunovski Alexandra; Josephson Anna; Bickford Paula C; Olson Lars ; Brene Stefan (Reprint)
AUTHOR ADDRESS: Karolinska Inst, Dept Neurosci, Retzius V 8, S-17177

Stockholm, Sweden**Sweden
AUTHOR E-MAIL ADDRESS: stefan.brene@ki.se
JOURNAL: Neuroreport 17 (9): p913-916 JUN 26 2006 2006
ISSN: 0959-4965
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The %%%Nogo%%% system has recently been implicated not only in regeneration but also in modulating plasticity. One reason for declining memory functions in aging may be altered plasticity in the aged hippocampus and cortex cerebri. Therefore, we have examined the levels of mRNA encoding %%%Nogo%%%, OMgp and MAG, as well as the receptor components NgR, %%%Lingo%%%-I and Troy in cortex and hippocampus of young (4 months), middle aged (16 months) and old (24 months) Fisher 344 rats. No significant changes of receptor components or the ligands OMgp or MAG were observed. %%%Nogo%%% mRNA, however, was significantly decreased in hippocampal subregions of aged animals. The specific decrease of %%%Nogo%%% mRNA levels in hippocampus and possibly cortex cerebri may relate to age-dependent decline of brain plasticity.

1/7/21
DIALOG(R)File 5:Biosis Previews(R)

18790830 BIOSIS NO.: 200600136225
Expression pattern of %%%LINGO%%%-1 in the developing nervous system of the chick embryo
AUTHOR: Okafuji Tatsuya (Reprint); Tanaka Hideaki
AUTHOR ADDRESS: Kumamoto Univ, Grad Sch Med Sci, Dept Dev Neurobiol, 1-1-1 Honjo, Kumamoto 8608556, Japan**Japan
AUTHOR E-MAIL ADDRESS: okafuji@kaiju.medic.kuamamoto-u.ac.jp
JOURNAL: Gene Expression Patterns 6 (1): p57-62 DEC 2005 2005
ISSN: 1567-133X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We isolated a chick homologue of %%%LINGO%%%-1 (cLINGO-1), a novel component of the %%%Nogo%%%-66 receptor (NgR)/p75 neurotrophin receptor (NTR) signaling complex, and examined the expression of cLINGO-1 in the developing brain and spinal cord of the chick embryo by in situ hybridization and immunohistochemistry. cLINGO-1 was expressed broadly in the spinal cord, including the ventral portion of the ventricular zone, and motor neurons. cLINGO-1 was also expressed in the dorsal root ganglion and boundary cap cells at dorsal and ventral roots. In the early embryonic brain, cLINGO-1 was first expressed in the prosencephalon and the ventral mesencephalon, and later in the telencephalon, the rostral part of the mesencephalon and some parts of the hindbrain. cLINGO-1 was also expressed in the ventral part of the neural retina and trigeminal and facial nerves. We also found that cLINGO-1, cNgR1 and p75NTR were expressed in overlapped patterns in the spinal cord and the dorsal root ganglion, but that these genes were expressed in distinct patterns in the early embryonic brain. (c) 2005 Elsevier B.V. All rights reserved.

1/7/22
DIALOG(R)File 5:Biosis Previews(R)

18590820 BIOSIS NO.: 200510285320
Multiple signals regulate axon regeneration through the %%%Nogo%%% receptor complex
AUTHOR: Yamashita Toshihide (Reprint); Fujitani Masashi; Yamagishi Satoru; Hata Katsuhiko; Mimura Fumiaki
AUTHOR ADDRESS: Chiba Univ, Grad Sch Med, Dept Neurobiol, Chuo Ku, 1-8-1 Inohana, Chiba 2608670, Japan**Japan
AUTHOR E-MAIL ADDRESS: t-yamashita@faculty.chiba-u.jp
JOURNAL: Molecular Neurobiology 32 (2): p105-111 OCT 2005 2005
ISSN: 0893-7648
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Several myelin-derived proteins have been identified as components of central nervous system (CNS) myelin, which prevents axonal regeneration in the adult vertebrate CNS. The discovery of the receptor for these proteins was a major step toward understanding the failure of axon regeneration. The receptor complex consists of at least three elements: the p75 receptor (p75(NTR)), the %%%Nogo%%% receptor and %%%LINGO%%%-1. Downstream from the receptor complex, RhoA activation has been shown to be a key element of the signaling mechanism of these proteins. Rho activation arrests axon growth, and blocking Rho activation promotes axon regeneration in vivo. Recent studies have identified conventional protein kinase C as an additional necessary component for axon growth inhibition. Possible crosstalk downstream of these signals should be explored to clarify all the inhibitory signals and may provide an efficient molecular target against injuries to the CNS.

1/7/23
DIALOG(R)File 5:Biosis Previews(R)

18535093 BIOSIS NO.: 200510229593
Ephrin-B3 is a myelin-based inhibitor of neurite outgrowth
AUTHOR: Benson M Douglas; Romero Mario I; Lush Mark E; Lu Q Richard; Henkemeyer Mark; Parada Luis F (Reprint)
AUTHOR ADDRESS: Univ Texas, SW Med Ctr, Ctr Dev Biol, 6000 Harry Hines Blvd, Dallas, TX 75390 USA**USA
AUTHOR E-MAIL ADDRESS: luis.parada@utsouthwestern.edu
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 102 (30): p10694-10699 JUL 26 2005 2005
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The inability of CNS axons to regenerate after traumatic spinal cord injury is due, in part, to the inhibitory effects of myelin. The three major previously identified constituents of this activity (%%%Nogo%%%, myelin-associated glycoprotein, and oligodendrocyte myelin glycoprotein) were isolated based on their potent inhibition of axon

outgrowth in vitro. All three myelin components transduce their inhibitory signals through the same %%%Nogo%%% receptor/p75 neurotrophin receptor/%%%LINGO%%%-1 (NgR1/p75/%%%LINGO%%%-1) complex. In this study, we considered that molecules known to act as repellants in vertebrate embryonic axonal pathfinding may also inhibit regeneration. In mice, ephrin-133 functions during development as a midline repellant for axons of the corticospinal tract. We therefore investigated whether this repellant was expressed in the adult spinal cord and retained inhibitory activity. We demonstrate that ephrin-133 is expressed in postnatal myelinating oligodendrocytes and, by using primary CNS neurons, show that ephrin-B3 accounts for an inhibitory activity equivalent to that of the other three myelin-based inhibitors, acting through p75, combined. Our data describe a known vertebrate axon guidance molecule as a myelin-based inhibitor of neurite outgrowth.

1/7/24
DIALOG(R)File 5:Biosis Previews(R)

18473556 BIOSIS NO.: 200510168056
Getting RIP'd stunts your growth
AUTHOR: Ceni Claire (Reprint); Barker Philip A
AUTHOR ADDRESS: McGill Univ, Montreal Neurol Inst, Ctr Neuronal Survival, 3801 Univ St, Montreal, PQ H3A 2B4, Canada**Canada
JOURNAL: Neuron 46 (6): p839-840 JUN 16 2005 2005
ISSN: 0896-6273
DOCUMENT TYPE: Article; Editorial
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The p75 neurotrophin receptor (p75NTR) collaborates with the %%%Nogo%%% receptor (NgR) and %%%LINGO%%%-1 to activate RhoA in response to myelin-based growth inhibitors such as myelin-associated glycoprotein (MAG). In this issue of Neuron, Domeniconi et al., in a surprising turn, show that MAG induces intramembrane proteolysis (RIP) of p75NTR and find that p75NTR cleavage is required for MAG-induced RhoA activation and growth inhibition.

1/7/25
DIALOG(R)File 5:Biosis Previews(R)

18265077 BIOSIS NO.: 200500171813
TAJ/TROY, an orphan TNF receptor family member, binds %%%Nogo%%%-66 receptor 1 and regulates axonal regeneration
AUTHOR: Shao Zhaohui; Browning Jeffrey L; Lee Xinhua; Scott Martin L; Shulga-Morskaya Sveltlana; Allaire Norm; Thill Greg; Levesque Melissa; Sah Dinah; McCoy John M; Murray Beth; Jung Vincent; Pepinsky R Blake; Mi Sha (Reprint)
AUTHOR ADDRESS: Dept Discovery Biol, Biogen Inc, 14 Cambridge Ctr, Cambridge, MA, 02142, USA**USA
AUTHOR E-MAIL ADDRESS: sha.mi@biogenidec.com
JOURNAL: Neuron 45 (3): p353-359 February 3, 2005 2005
MEDIUM: print
ISSN: 0896-6273 _(ISSN print)

DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Myelin-associated inhibitory factors (MAIFs) are inhibitors of CNS axonal regeneration following injury. The %%%Nogo%%% receptor complex, composed of the Nogo66 receptor 1 (NgR1), neurotrophin p75 receptor (p75), and %%%LINGO%%%-1, represses axon regeneration upon binding to these myelin components. The limited expression of p75 to certain types of neurons and its temporal expression during development prompted speculation that other receptors are involved in the NgR1 complex. Here, we show that an orphan receptor in the TNF family called TAJ, broadly expressed in postnatal and adult neurons, binds to NgR1 and can replace p75 in the p75/NgR1/%%%LINGO%%%-1 complex to activate RhoA in the presence of myelin inhibitors. In vitro exogenously added TAJ reversed neurite outgrowth caused by MAIFs. Neurons from Taj-deficient mice were more resistant to the suppressive action of the myelin inhibitors. Given the limited expression of p75, the discovery of TAJ function is an important step for understanding the regulation of axonal regeneration.

1/7/26
DIALOG(R)File 5:Biosis Previews(R)

18265076 BIOSIS NO.: 200500171812
A TNF receptor family member, TROY, is a coreceptor with %%%Nogo%%% receptor in mediating the inhibitory activity of myelin inhibitors
AUTHOR: Park Jong Bae; Yiu Glenn; Kaneko Shinjiro; Wang Jing; Chang JuFang; He Zhigang (Reprint)
AUTHOR ADDRESS: Childrens HospSch MedDiv Neurosci, Harvard Univ, Boston, MA, 02115, USA**USA
AUTHOR E-MAIL ADDRESS: zhigang.he@childrens.harvard.edu
JOURNAL: Neuron 45 (3): p345-351 February 3, 2005 2005
MEDIUM: print
ISSN: 0896-6273 _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A major obstacle for successful axon regeneration in the adult central nervous system (CNS) arises from inhibitory molecules in CNS myelin, which signal through a common receptor complex on neurons consisting of the ligand-binding %%%Nogo%%%-66 receptor (NgR) and two transmembrane coreceptors, p75 and %%%LINGO%%%-1. However, p75 expression is only detectable in sub-populations of mature neurons, raising the question of how these inhibitory signals are transduced in neurons lacking p75. In this study, we demonstrate that TROY (also known as TAJ), a TNF receptor family member selectively expressed in the adult nervous system, can form a functional receptor complex with NgR and %%%LINGO%%%-1 to mediate cellular responses to myelin inhibitors. Also, both overexpressing a dominant-negative TROY or presence of a soluble TROY protein can efficiently block neuronal response to myelin inhibitors. Our results implicate TROY in mediating myelin inhibition, offering new insights into the molecular mechanisms of regeneration failure in the adult nervous system.

1/7/27
DIALOG(R)File 5:Biosis Previews(R)

18171455 BIOSIS NO.: 200500078520
Neuronal activity-induced regulation of %%%Lingo%%%-I
AUTHOR: Trifunovski Alexandra (Reprint); Josephson Anna; Ringman Andreas; Brene Stefan; Spenger Christian; Olson Lars
AUTHOR ADDRESS: Dept Neurosci, Karolinska Inst, S-17177, Stockholm, Sweden **Sweden
AUTHOR E-MAIL ADDRESS: Alexandra.Trifunovski@neuro.ki.se
JOURNAL: Neuroreport 15 (15): p2397-2400 October 25, 2004 2004
MEDIUM: print
ISSN: 0959-4965 _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Axonal regeneration after injury can be limited in the adult CNS by the presence of inhibitory proteins such as %%%Nogo%%%. %%%Nogo%%% binds to a receptor complex that consists of %%%Nogo%%% receptor (NgR), p75NTR, and %%%Lingo%%%-1. %%%Nogo%%% binding activates RhoA, which inhibits axonal outgrowth. Here we assessed %%%Lingo%%%-1 and NgR mRNA levels after delivery of BDNF into the rat hippocampal formation, %%%Lingo%%%-1 mRNA levels in rats subjected to kainic acid (KA) and running in running wheels. %%%Lingo%%%-1 mRNA was not changed by running. However, we found that %%%Lingo%%%-1 mRNA was strongly up-regulated while NgR mRNA was down-regulated in the dentate gyrus in both the BDNF and the KA experiments. Our data demonstrate inverse regulation of NgR and %%%Lingo%%%-1 in these situations, suggesting that %%%Lingo%%%-1 up-regulation is one characteristic of activity-induced neural plasticity responses.

1/7/28
DIALOG(R)File 5:Biosis Previews(R)

18169073 BIOSIS NO.: 200500076138
Segregation of Nogo66 receptors into lipid rafts in rat brain and inhibition of Nogo66 signaling by cholesterol depletion
AUTHOR: Yu Weiying; Guo Wei; Feng Linyin (Reprint)
AUTHOR ADDRESS: Shanghai Inst Biol SciShanghai Inst Mat Med, Chinese Acad Sci, Shanghai, 201203, China**China
AUTHOR E-MAIL ADDRESS: lyfeng@sibs.ac.cn
JOURNAL: FEBS Letters 577 (1-2): p87-92 November 5, 2004 2004
MEDIUM: print
ISSN: 0014-5793
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: NogoA, a myelin-associated component, inhibits neurite outgrowth. Nogo66, a portion of NogoA, binds to Nogo66 receptor (NgR) and induces the inhibitory signaling. %%%LINGO%%%-1 and p75 neurotrophin receptor

(p75), the low-affinity nerve growth factor receptor, are also required for NogoA signaling. However, signaling mechanisms downstream to %%%Nogo%%% receptor remain poorly understood. Here, we observed that NgR and p75 were colocalized in low-density membrane raft fractions derived from forebrains and cerebella as well as from cerebellar granule cells. NgR interacted with p75 in lipid rafts. In addition, disruption of lipid rafts by beta-methylcyclodextrin, a cholesterol-binding reagent, reduced the Nogo66 signaling. Our results suggest an important role of lipid rafts in facilitating the interaction between NgRs and provide insight into mechanisms underlying the inhibition of neurite outgrowth by NogoA.

1/7/29
DIALOG(R)File 5:Biosis Previews(R)

17791487 BIOSIS NO.: 200400158828
%%%LINGO%%%-1 is a component of the %%%Nogo%%%-66 receptor/p75 signaling complex.
AUTHOR: Mi Sha (Reprint); Lee Xinhua; Shao Zhaohui; Thill Greg; Ji Benxiu; Relton Jane; Levesque Melissa; Allaire Norm; Perrin Steve; Sands Bryan; Crowell Thomas; Cate Richard L; McCoy John M; Pepinsky R Blake
AUTHOR ADDRESS: Department of Discovery Biology, Biogen Idec, Inc., 14 Cambridge Center, Cambridge, MA, 02142, USA**USA
AUTHOR E-MAIL ADDRESS: sha.mi@biogenidec.com
JOURNAL: Nature Neuroscience 7 (3): p221-228 March 2004 2004
MEDIUM: print
ISSN: 1097-6256 _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Axon regeneration in the adult CNS is prevented by inhibitors in myelin. These inhibitors seem to modulate RhoA activity by binding to a receptor complex comprising a ligand-binding subunit (the %%%Nogo%%%-66 receptor NgR1) and a signal transducing subunit (the neurotrophin receptor p75). However, in reconstituted non-neuronal systems, NgR1 and p75 together are unable to activate RhoA, suggesting that additional components of the receptor may exist. Here we describe %%%LINGO%%%-1, a nervous system-specific transmembrane protein that binds NgR1 and p75 and that is an additional functional component of the NgR1/p75 signaling complex. In non-neuronal cells, coexpression of human NgR1, p75 and %%%LINGO%%%-1 conferred responsiveness to oligodendrocyte myelin glycoprotein, as measured by RhoA activation. A dominant-negative human %%%LINGO%%%-1 construct attenuated myelin inhibition in transfected primary neuronal cultures. This effect on neurons was mimicked using an exogenously added human %%%LINGO%%%-1-Fc fusion protein. Together these observations suggest that %%%LINGO%%%-1 has an important role in CNS biology.
? log y
19nov08 17:47:39 User217744 Session D1174.3
$3.35 0.542 DialUnits File5
$70.76 29 Type(s) in Format 7
$70.76 29 Types
$74.11 Estimated cost File5

```
     $0.53  TELNET
    $74.64  Estimated cost this search
    $74.64  Estimated total session cost   0.928 DialUnits
Logoff: level 05.22.00 D  17:47:39
```